Pharmaceutical Synthesis and Fine Particle Formation Using Carbon Dioxide-Assisted Aerosolization and Bubble Drying

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The production of inhalable dry powders of pharmaceuticals can be achieved using a recently invented supercritical or near-critical CO_2-assisted aerosolization and bubble drying process [1,2]. This technique utilizes the high solubility of liquid carbon dioxide in water, coupled with expansion of the solution through a restrictor, as a means to aerosolize aqueous solutions of drugs. When the droplets are dried, the particles are typically spherical and have diameters in the 0.5 to 5 micron size range, which makes them suitable for inhalation to treat pulmonary and other diseases. The particles can be hollow or solid, as observed by transmission electron microscopy (TEM). The nebulization process is highly effective due to the production of active small bubbles of CO_2 gas surrounded by a water-drug film. The evolution of CO_2 gas may aid in the breakup of water droplets to produce even finer particles. Efficient aerosolization to form small bubbles and droplets allows for more rapid particle drying at lower temperatures (e.g., 25 to 70˚C) than can typically be achieved with conventional spray-drying techniques, which will constitute an advantage in pharmaceutical processing. As a result, the technique is well-suited for the processing of proteins that might otherwise be damaged under harsher conditions of other particle formation processes (higher temperatures, localized heating, etc.). Current investigations are focused on stabilizing protein powders by adding sugars and surfactants. Residual moisture contents of 1% and less have been achieved with the system in drying various lysozyme formulations.

[1] R.E. Sievers and U. Karst, U.S. Patent 5,639,441, (1997).
[2] R.E. Sievers, U. Karst, P.D. Milewski, S.P. Sellers, B.A. Miles, J.D. Schaefer, C.R. Stoldt, and C.Y. Xu, *Aerosol. Sci., and Tech*. **30**, 3 (1999).